Pediatr Neonatol 2010;51(5):292–295

ELSEVIER

CASE REPORT

Ocular Findings in a Case of Trisomy 18 With Variant of Dandy-Walker Syndrome

Fong-Fong Lim[1,2], Yan-Yan Ng[1,2], Jui-Ming Hu[1,2], Suh-Jen Chen[1], Pen-Hua Su[1,2,3]*, Jia-Yuh Chen[2,3]

[1]*Division of Genetics, Department of Pediatrics, Chung Shan Medical University Hospital, Taichung, Taiwan*
[2]*Division of Neonatology, Department of Pediatrics, Chung Shan Medical University Hospital, Taichung, Taiwan*
[3]*School of Medicine, Chung Shan Medical University, Taichung, Taiwan*

Received: Mar 20, 2009
Revised: Oct 13, 2009
Accepted: Nov 12, 2009

KEY WORDS:
Dandy-Walker variant;
disc coloboma;
persistent papillary membrane;
retinal dysplasia;
trisomy 18

Trisomy 18 is the second most common chromosomal syndrome and has multiple dysmorphic features. However, ocular findings in trisomy 18 are rarely reported. Retinal folds are the most common ocular finding described to date, although retinal hypopigmentation, dysplasia, and areas of hemorrhage and gliosis are also found in trisomy 18. Dandy-Walker syndrome is a brain malformation that has been reported in association with numerous chromosomal abnormalities, although it has rarely been reported in association with trisomy 18. Here, we present a case of trisomy 18 with ocular pathology and variant of Dandy-Walker syndrome, a combination that has not previously been reported.

1. Introduction

Trisomy 18, also known as Edwards syndrome, is one of the most common numerical chromosomal disorders. The incidence of trisomy 18 is approximately 1 in 6000 live births. It is associated with a high rate of intrauterine death, and 95% of live-born infants with trisomy 18 die within 1 year.[1]

Typical abnormalities of trisomy 18 include small, premature appearance, a prominent occiput, clenched hands with a tendency for the index finger to overlap the third finger, the fifth finger to overlap the fourth finger, a short sternum, and low arch dermal ridge patterning on the fingertips.[2]

The Dandy-Walker malformation (DWM) consists of an enlarged posterior fossa with a high position of the tentorium, hypogenesis or agenesis of the cerebellar vermis, and a cystic dilatation of the fourth ventricle that fills nearly the entire posterior fossa.[3] DWM has been reported in a wide variety of syndromes, including chromosomal anomalies and antenatal exposure to teratogens.[4] Twenty cases of trisomy 18 associated with Dandy-Walker syndrome have been reported,[5–7] but only three of these cases were reported in detail.[5,6]

Ocular findings have been described in fewer than 10% of trisomy 18 cases. Retinal folds were the most common histopathologic finding in the cases

*Corresponding author. Division of Genetics, Department of Pediatrics, Chung Shan Medical University Hospital, 110 Chien-Kuo North Road, Section 1, Taichung 402, Taiwan.
E-mail: jen@csh.org.tw

reviewed. Other common retinal observations include hypopigmentation of the posterior pigment epithelium, dysplasia, and areas of hemorrhage and gliosis.[8] Here, we present a case of trisomy 18 with DWM and multiple abnormal ocular findings.

2. Case Report

A female neonate was born by cesarean section to a healthy 31-year-old woman, gravida 2 para 1, at 37 weeks of gestational age. Birth weight was 1448 g. The mother had received regular prenatal care, and intrauterine growth restriction with small placenta was noted by prenatal ultrasound at 30 weeks of gestation. Family history was unremarkable for congenital abnormalities, and an older sibling was normal. The patient's Apgar scores were 6 at 1 minute and 7 at 5 minutes. She was transferred to our neonatal intensive care unit for respiratory distress and intrauterine growth restriction. The baby's ponderal index was 2.64, which was between the 10th and 90th percentile. Her length was 38 cm, head circumference was 29 cm, and chest circumference was 26 cm; these measurements were all below the 5th percentile.

Physical examination revealed multiple congenital anomalies, including a prominent occiput, a short sternum (Figure 1A) of 4 cm in length (normal length: 5–6 cm) (Figure 1B), preaxial polydactyly (Figure 2A), clenched hands with overlapping of the index and fourth fingers over the third finger (Figure 2B), single transverse palmar crease, rocker bottom feet (Figure 2C), and a prominent clitoris. The patient's eyes had small pupils with irregular margins, surrounded by reddish pigmentation (Figure 3A). A detailed ophthalmic examination was performed. The corneas measured 8 mm bilaterally (normal range: 10–12 mm). The lens was clear without cataracts. No iris coloboma was noted except for iris depigmentation with persistent pupillary membrane with a swallow anterior chamber. Both optic discs showed inferior coloboma (the right side being larger than left side; Figures 3B and 3C). Retinal dysplasia was also noted in both eyes.

Ultrasound of the brain revealed thinning of the corpus callosum, cerebellar hypoplasia, and a small gyrus volume. Magnetic resonance imaging (MRI) of the brain revealed a small head size and mild brachycephaly, Dandy-Walker variant (vermian-cerebellar hypoplasia) (Figure 4), and brain infarction in the right cerebral hemisphere. Echocardiography showed a double outlet right ventricle, a ventricular septal defect, coarctation of the aorta, engorgement of the main pulmonary artery, and a huge patent ductus arteriosus, in addition to congestive heart failure. Sonograms of the liver, spleen, and kidney were normal. Cytogenetic analysis showed 47, XX, +18. The infant was not mechanically ventilated and she died of cardiopulmonary failure at 94 days of age. An autopsy was not performed.

3. Discussion

Trisomy 18 is one of the most common chromosomal disorders and the second most common autosomal trisomy (after trisomy 21) in newborns. The most common dysmorphic features associated with trisomy 18 are well documented, and include abnormal appearances of the face and limbs. Abnormalities of the cardiovascular system (ventricular septal defect in 94%, patent ductus arteriosus in 77%, and atrial septal defect in 68% as reported by Lin et al[9]) and central nervous system are very common, as are renal and gastrointestinal abnormalities. The most

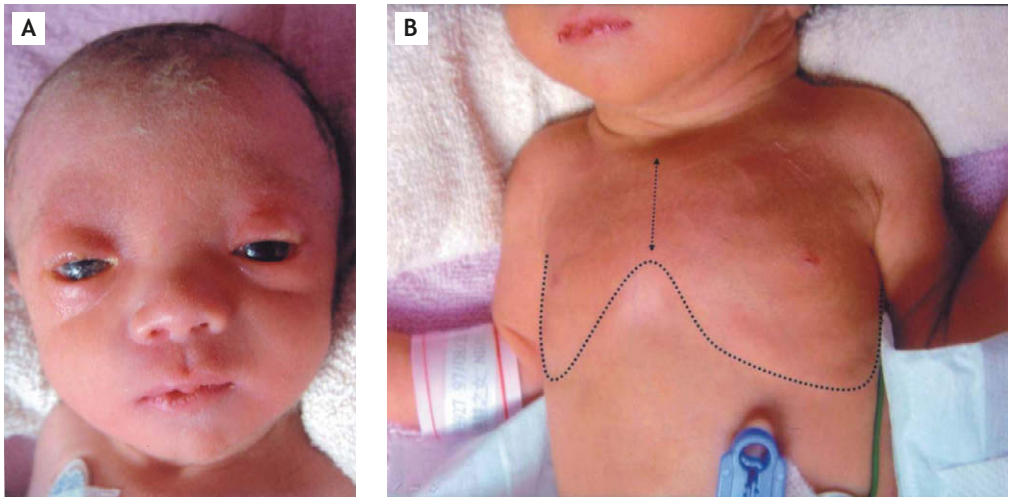

Figure 1 (A) Facial appearance and (B) short sternum of our patient.

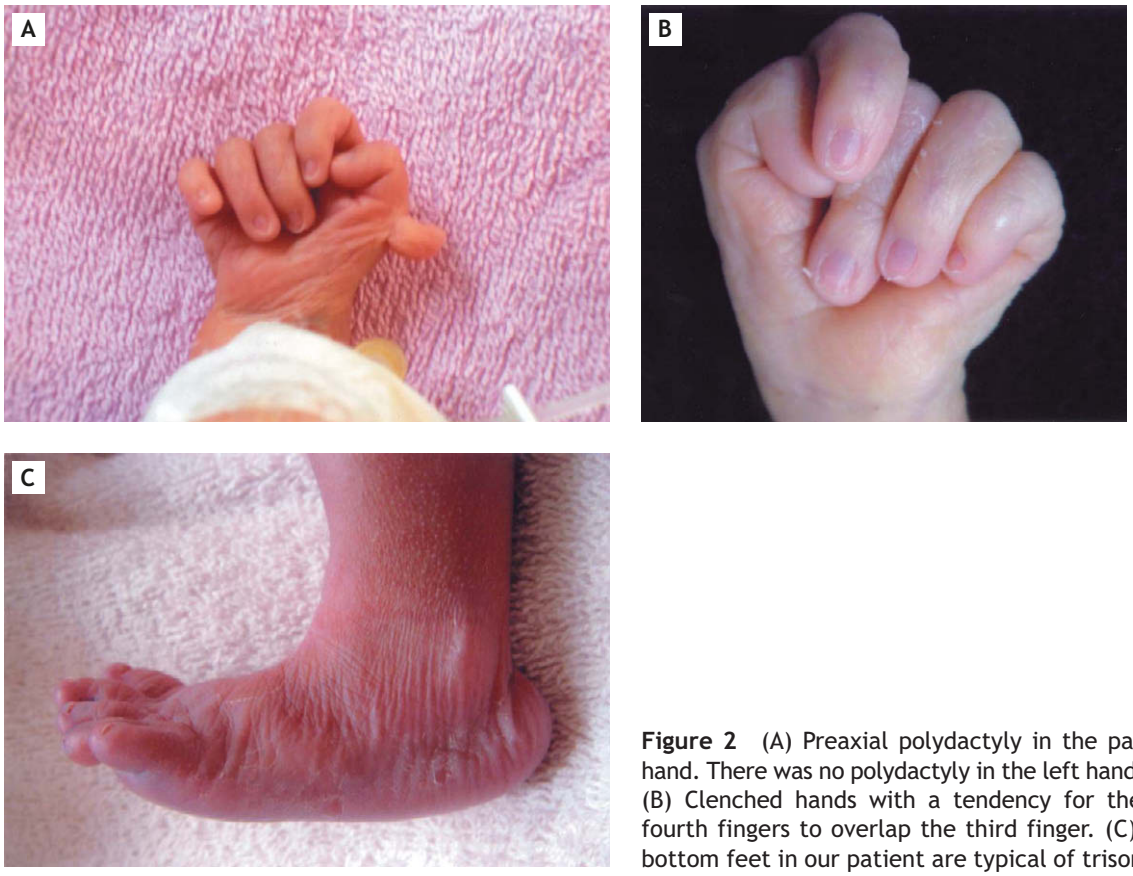

Figure 2 (A) Preaxial polydactyly in the patient's right hand. There was no polydactyly in the left hand or the feet. (B) Clenched hands with a tendency for the index and fourth fingers to overlap the third finger. (C) The rocker bottom feet in our patient are typical of trisomy 18.

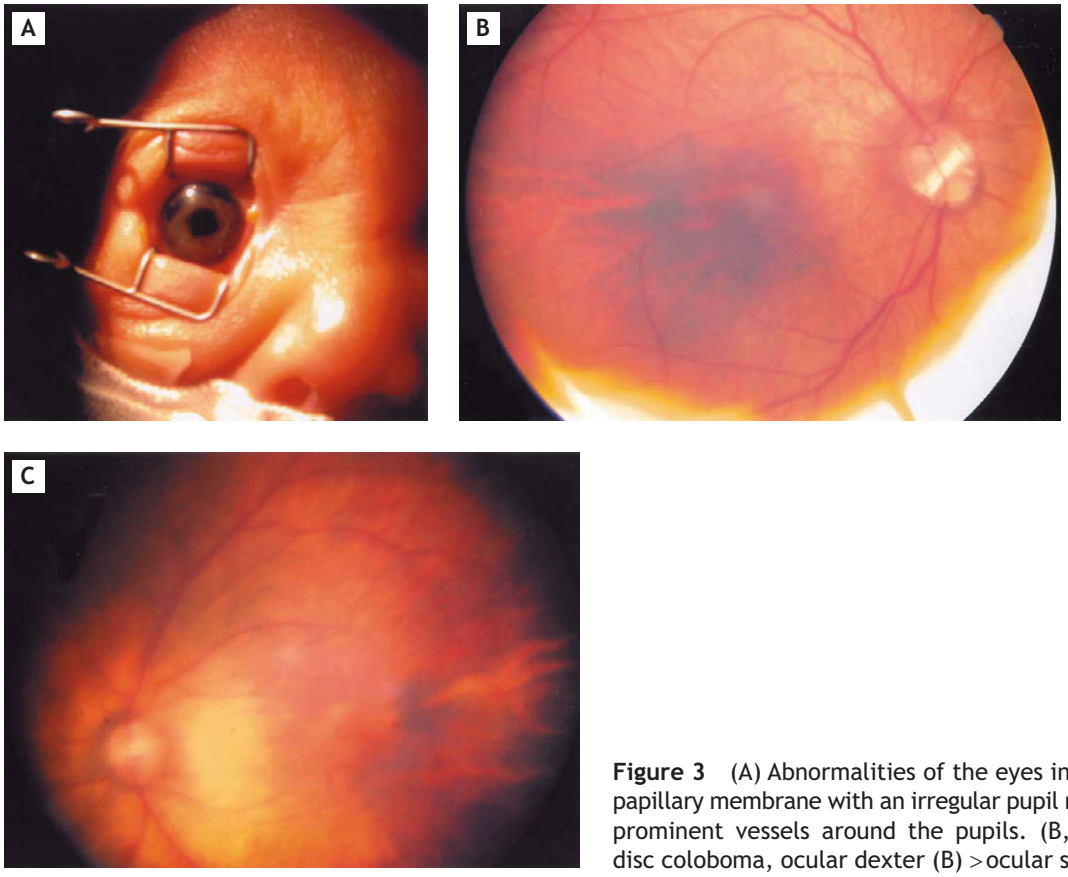

Figure 3 (A) Abnormalities of the eyes include a persistent papillary membrane with an irregular pupil margin and reddish prominent vessels around the pupils. (B,C) Bilateral optic disc coloboma, ocular dexter (B) >ocular sinister (C).

Figure 4 Brain magnetic resonance images revealed a normal-sized posterior fossa with a relatively symmetrical decrease in size of the cerebellum, a predominant cerebellar inferior vermis, and prominent retrocerebellar cerebrospinal fluid space. These findings prompted the diagnosis of Dandy-Walker syndrome variant.

commonly reported brain anomalies (identified by cranial ultrasound) are cerebellar hypoplasia (32%), brain edema (29%), enlarged cisterna magna (26%) and choroid plexus cysts (19%).[9]

DWM refers to the absence or hypoplasia of the cerebellar vermis, cystic dilatation of the fourth ventricle, and enlargement of the posterior fossa. DWM has been reported in association with a variety of other malformation syndromes. Complications include deformation of the central nervous system, hyperdactylia, syndactyly, cleft palate, alloplasia of kidneys, liver and pancreas, and abnormal retinas.[10]

The incidence of DWM is lower than 6% among patients with trisomy 18. MRI of our patient revealed a normal-sized posterior fossa with a relatively symmetrical decrease in the size of the cerebellum, predominance of the cerebellar inferior vermis and prominent retrocerebellar cerebrospinal fluid space, favoring a variant of Dandy-Walker syndrome (vermian-cerebellar hypoplasia). In contrast to the brain echography examination of our case, which showed thinning of the corpus callosum, cerebellar hypoplasia, and a small gyrus volume for her gestational age, the presence of Dandy-Walker syndrome variant may be underestimated if MRI is not performed. Therefore, brain MRI is recommended for diagnosis in these cases.

In addition to DWM, ocular finding are rarely reported in trisomy 18. Calderone et al[8] reviewed the available literature and found that in several hundred case reports of trisomy 18, only 13 articles mentioned ocular pathology, and only 5 covered this subject in any detail. Lin et al[9] reported abnormal eye structures in 6 of the 39 patients (16%) with trisomy 18; they reported 13% of patients (5/39) with corneal opacity and 8% (3/39) with micropthalmia.

The most commonly affected ocular structures include the cornea, anterior uveal tract, lens, and retina. Our patient had no cataracts or iris coloboma, except for depigmentation of the iris with persistent pupillary membrane and a swallow anterior chamber. Both eyes showed optic disc coloboma and retinal dysplasia. The most common ophthalmic finding in trisomy 18 is retinal dysplasia, followed by hypopigmentation of posterior pigment epithelium, dysplasia, and areas of hemorrhage and gliosis. Two other relatively common findings include cataracts and ciliary process anomalies of the uveal tract.[7]

The relatively low incidence of ocular findings may reflect incomplete reporting, because ocular findings are not diagnostic for trisomy 18. Trisomies 13 and 21 have also been reported to have intraocular anomalies. Thus further evaluation of ophthalmic anomalies may be helpful in trisomy 18 and other chromosomal disorders to provide more precise information.

Trisomy 18 is a chromosomal disorder that results in complex abnormalities. The incidence of each abnormality is now well established based on the literature published to date. However, the DWM and ophthalmic anomalies may have been underestimated because of a lack of modern instruments or the inconvenience associated with further examinations.

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